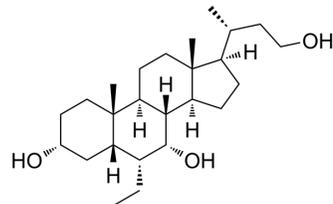


BAR502

| | | | |
|---------------------------|--|-------|---------|
| Cat. No.: | HY-101273 | | |
| CAS No.: | 1612191-86-2 | | |
| Molecular Formula: | C ₂₅ H ₄₄ O ₃ | | |
| Molecular Weight: | 392.62 | | |
| Target: | G protein-coupled Bile Acid Receptor 1; FXR; Autophagy | | |
| Pathway: | GPCR/G Protein; Metabolic Enzyme/Protease; Autophagy | | |
| Storage: | Powder | -20°C | 3 years |
| | | 4°C | 2 years |
| | In solvent | -80°C | 2 years |
| | | -20°C | 1 year |



SOLVENT & SOLUBILITY

In Vitro

DMF : 50 mg/mL (127.35 mM; Need ultrasonic)
 Ethanol : ≥ 50 mg/mL (127.35 mM)
 * "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Solvent Concentration | Mass | | |
|---------------------------|-----------------------|-----------|------------|------------|
| | | 1 mg | 5 mg | 10 mg |
| | 1 mM | 2.5470 mL | 12.7350 mL | 25.4699 mL |
| | 5 mM | 0.5094 mL | 2.5470 mL | 5.0940 mL |
| | 10 mM | 0.2547 mL | 1.2735 mL | 2.5470 mL |

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

In Vivo

- Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (6.37 mM); Clear solution
- Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (6.37 mM); Clear solution
- Add each solvent one by one: 10% EtOH >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (6.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAR502 is a dual FXR and GPBAR1 agonist with IC₅₀ values of 2 μM and 0.4 μM, respectively.

IC₅₀ & Target

IC₅₀: 2 μM (FXR), 0.4 μM (GPBAR1)^[1]

In Vitro

BAR502 is a truncated side chain alcohol with both substituents on ring B in α-configuration. At the concentration of 10 μM,

BAR502 fails to transactivate GR, PPAR γ , and LXR, respectively, but it transactivates the nuclear receptor PXR. BAR502 is able to induce the expression of pro-glucagon mRNA in GLUTAg cells, an intestinal endocrine cell line, as well as to increase cAMP concentrations in THP-1 cells. BAR502 induces the expression of OST α , BSEP, and SHP in HepG2 cells. BAR502 shows a very potent activity in the recruitment of SRC-1 coactivator and high affinity to FXR^[1].

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

In Vivo

Treatment with BAR502 causes a 10% reduction of b.w., increases insulin sensitivity and circulating levels of HDL, while reduces steatosis, inflammatory and fibrosis scores and liver expression of SREPB1c, FAS, PPAR γ , CD36 and CYP7A1 mRNA. BAR502 increases the expression of SHP and ABCG5 in the liver and SHP, FGF15 and GLP1 in intestine. BAR502 promotes the browning of epWAT and reduces liver fibrosis induced by CCl₄^[2]. In models of non-obstructive cholestasis, BAR502 attenuates liver injury without causing itching. Co-treatment with BAR502 increases survival, attenuates serum alkaline phosphatase levels and robustly modulates the liver expression of canonical FXR target genes including OST α , BSEP, SHP and MDR1, without inducing pruritus^[3].

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

PROTOCOL

Animal Administration ^[2]

Mice: C57BL6 mice 24 weeks old are fed a high fat diet containing 60% kJ fat and fructose in drinking water (42 g/L) or normal diet (6 mice) for 18 weeks. After 10 weeks of HFD, mice are randomized to receive HFD alone (9 mice) or HFD plus BAR502 (15 mg/kg/day) body weight by gavage (9 mice) for 8 weeks. Mice are housed under controlled temperatures (22 °C) and photoperiods (12:12-hour light/dark cycle), allowed unrestricted access to standard mouse chow and tap water and allowed to acclimate to these conditions for at least 5 days before inclusion in an experiment^[2].

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

REFERENCES

[1]. Festa C, et al. Exploitation of cholane scaffold for the discovery of potent and selective farnesoid X receptor (FXR) and G-protein coupled bile acid receptor 1 (GP-BAR1) ligands. *J Med Chem.* 2014 Oct 23;57(20):8477-95.

[2]. Carino A, et al. BAR502, a dual FXR and GPBAR1 agonist, promotes browning of white adipose tissue and reverses liver steatosis and fibrosis. *Sci Rep.* 2017 Feb 16;7:42801.

[3]. Cipriani S, et al. Impaired Itching Perception in Murine Models of Cholestasis Is Supported by Dysregulation of GPBAR1 Signaling. *PLoS One.* 2015 Jul 15;10(7):e0129866.

Caution: Product has not been fully validated for medical applications. For research use only.

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