Product Data Sheet

Chemical Properties

Product Name: Bardoxolone methyl
Cas No.: 218600-53-4
M.Wt: 505.69
Formula: C32H43NO4
Synonyms: NSC 713200; RTA 402; CDDO Methyl ester
Chemical Name: methyl (4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,7,8,8a,14a,14b-decahydropicene-4a-carboxylate
Canonical SMILES: CC1(CCC2(CCC3(C(C2C1)C(=O)C=C4C3(CCC5C4(C=C(C(=O)C5(C)C)C#N)C)C)C)C(=O)OC)C
Solubility: ≥25.3mg/mL in DMSO
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Chromatin/Epigenetics
Pathways: JAK
Description: Bardoxolone methyl is an activator of the KEAP1-Nrf2 pathway [1] and also inhibits the pro-inflammatory transcription factor NF-κB [2] which can protect kidneys from aristolochic acid.
(AA)-induced acute kidney injury (AKI) with IC50 value of 1.5 nM and LC50 value of 2.1 µM [3]. Nrf2, a transcription factor, is a basic leucine zipper (bZIP) protein that regulates the expression of antioxidant proteins that protect against oxidative damage triggered by injury and inflammation [4], such as NADPH, Glutathione, SRXN1, TXNRD1, HMOX1, GST, UGT and Mrps. Nrf2 plays an important role in the maintenance of homeostasis which can control the basal and inducible expression of a battery of genes with diverse physiological roles, including the preservation of redox balance, the metabolism and detoxification of xenobiotics, and the regulation of multiple metabolic pathways that ensure the provision of cellular energy[5].

Bardoxolone methyl is a synthetic oleanane triterpenoid compound, which has no effect on the function and histology of normal kidneys but increased renal expression of Nrf2, HO-1 and NQO1 by western blotting analysis of mice kidneys and immunofluorescence staining, and can prevent AA-induced acute kidney injury and reduce AAI-induced TI injury in mRNA and protein levels through real-time PCR.[6] In conclusion, Bardoxolone methyl can prevent AAI-induced renal damage, and it may exert this renoprotective effects by activating the Nrf2 signaling pathway and inducing the downstream target genes expression. A phase 3 clinical trial evaluating bardoxolone methyl for the treatment of chronic kidney disease (CKD) was terminated in October 2012 after patients treated with the drug were found to have experienced a higher rate of heart-related adverse events, including heart failure, hospitalizations and deaths.[7] Now in 2014, Kyowa Hakko Kirin announced plans to evaluate both safety and efficacy of bardoxolone methyl in a Phase 2 clinical study to be performed in Japan for the treatment of CKD associated with type 2 diabetes.[8]

Reference:

Protocol

Cell experiment:

Cell lines  
HL-60, KG-1 and NB4 cells
Preparation method

The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions

~ 5 μM; 72 hrs

Applications

In leukemia cells, such as HL-60, KG-1, and NB4 cells, Bardoxolone Methyl decreased cell viability with the IC50 values of 0.4, 0.4 and 0.27 μM, respectively.

**Animal experiment [3]:**

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Female A/J mice i.p. injected with vinyl carbamate</th>
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<tbody>
<tr>
<td>Dosage form</td>
<td>60 or 400 mg/kg; p.o.; the mice fed Bardoxolone Methyl for 2 weeks and then switched to a week of control diet, for 15 weeks.</td>
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<tr>
<td>Applications</td>
<td>At the dose of 60 mg, Bardoxolone Methyl reduced the number, size, as well as severity of lung tumors in vivo.</td>
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<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
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</table>

**Reference:**


**Caution**
Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.