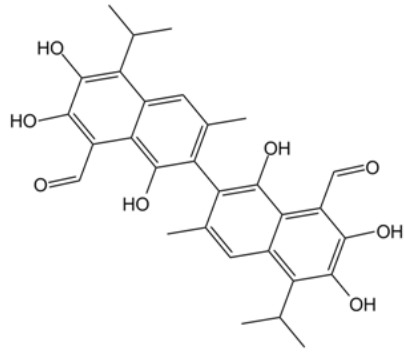
Product Data Sheet

Chemical Properties



Product Name: AT-101

Cas No.: 90141-22-3

M.Wt: 518.55

Formula: C30H30O8

Synonyms: (R)-(-)-Gossypol;R-(-)-gossypol acetic acid;AT 101;AT101

Chemical Name: 7-(8-formyl-1,6,7-trihydroxy-3-methyl-5-propan-2-ylnaphthalen-2-yl)-2,3,8-trihydroxy-6-methyl-4-propan-2-ylnaphthalene-1-carbaldehyde

Canonical SMILES: CC1=C(C(=C2C(=C1)C(=C(C(=C2C=O)O)O)C(C)C)O)C3=C(C=C4C(=C3O)C(=C(C(=C4C(C)C)O)O)C=O)C

Solubility: Soluble in DMSO > 10 mM

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 : Apoptosis

Pathways: Bcl-2 Family

Description:

AT101, a natural product from cottonseed with a BH3-mimetic structure, was identified as a small molecule inhibitor of Bcl-2/Bcl-xL/Mcl-1 that potently induces apoptosis in various cancer cell lines [1].It is one of the world's first small molecule Bcl-2 inhibitors that has entered into clinical

trials and is now in phase II clinical trials for hormone-refractory prostate cancer and other types of cancers [2, 3]. Few side effects of gossypol have been reported, with the major side effects of gossypol being nausea and vomiting in the third month of treatment or rashes earlier in the course of treatment [4]. Thus, AT101 is clinically safe [2, 3] and could be used as a potential inducer of apoptosis in cancer treatment.

As a BH3 mimetic, AT-101 binds to the hydrophobic surface binding groove BH3 of the anti-apoptotic proteins Bcl-2 and Bcl-xL, blocking their heterodimerization with pro-apoptotic members of the Bcl-2 family of proteins such as Bad, Bid, and Bim; this may result in the inhibition of tumor cell proliferation and the induction of tumor cell apoptosis. Preclinical studies revealed that gossypol not only interrupts the interaction between anti- and proapoptotic Bcl-2 family proteins but also induces BH3 protein (such as Puma and Noxa) up-regulation or down-regulates XIAP expression [5]. Thus, gossypol can induce apoptosis by activating apoptogenic factors other than the Bcl-2 family. AT-101 induced apoptosis in vitro through activation of caspase-9.

AT101 delayed onset of androgen-independent growth of VCaP prostate cancer xenografts in vivo. Gossypol can neutralize antiapoptotic Bcl-2 proteins and induced Bax activation [1]. However, the function of gossypol was not limited to effects on the interaction between anti- and proapoptotic Bcl-2 proteins. Some studies have demonstrated that gossypol could down-regulate Bcl-2, Bcl-xL, and XIAP expression [6] or induce Puma and Noxa expression. Therefore, the apoptotic effect of gossypol has been demonstrated to be attenuated by the presence of androgen in a prostate cancer xenograft mouse model.

***Reference**:*

[1]. Meng Y, Tang W,Dai Y, et al. Natural BH3-mimetic (-)-gossypol chemosensitizes human prostate cancer via Bcl-xL inhibition accompanied by increase of Puma and Noxa.Molecular cancer therapeutics,2008,7(7): 2192–2202.

[2]. Liu G,Kelly W. K,Wilding G,et al. An Open-Label, Multicenter, Phase I/II Study of Single-Agent AT-101 in Men with Castrate-Resistant Prostate Cancer (CRPC).Clinical Cancer Research,2009,15(9): 3172–3176.

[3]. Van Poznak C, Seidman A. D,Reidenberg M,et al. Oral gossypol in the treatment of patients with refractory metastatic breast cancer: a phase I/II clinical trial,Breast Cancer ResTreat ,2001,66(3):239-48.

[4]. Qiu J,Levin L. R,Buck J,et al. Different pathways of cell killing by gossypol enantiomers.Exp Biol Med (Maywood) ,2002,227(6):398-401.

[5]. Balakrishnan K,Burger J. A,Wierda W. G,et al. AT-101 induces apoptosis in CLL B cells and overcomes stromal cell–mediated Mcl-1 induction and drug resistance.Blood,2009,113(1): 149–153.

[6].Sung B,Ravindran J,Prasad S,et al.Gossypol Induces Death Receptor-5 through Activation of the ROS-ERK-CHOP Pathway and Sensitizes Colon Cancer Cells to TRAIL.J Biol Chem,2010,285(46): 35418–35427.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

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. Shortterm 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.

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