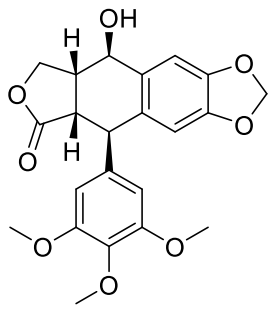
Product data sheet

MedKoo Cat#: 205812 Name: Picropodophyllin CAS#: 477-47-4 Chemical Formula: $C_{22}H_{22}O_8$ Exact Mass: 414.13147 Molecular Weight: 414.41	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Picropodophyllin, also known as Picropodophyllotoxin, AXL1717 or PPP, is a cyclolignan alkaloid found in the mayapple plant family (Podophyllum peltatum), and a small molecule inhibitor of the insulin-like growth factor 1 receptor (IGF1R) with potential antineoplastic activity. Picropodophyllin specifically inhibits the activity and downregulates the cellular expression of IGF1R without interfering with activities of other growth factor receptors, such as receptors for insulin, epidermal growth factor, platelet-derived growth factor, fibroblast growth factor and mast/stem cell growth factor (KIT). This agent shows potent activity in the suppression of tumor cell proliferation and the induction of tumor cell apoptosis.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	15.0	36.2

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.41 mL	12.07 mL	24.13 mL
5 mM	0.48 mL	2.41 mL	4.83 mL
10 mM	0.24 mL	1.21 mL	2.41 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Tarnowski M, Tkacz M, Zgutka K, Bujak J, Kopytko P, Pawlik A. Picropodophyllin (PPP) is a potent rhabdomyosarcoma growth inhibitor both in vitro and in vivo. BMC Cancer. 2017 Aug 9;17(1):532. doi: 10.1186/s12885-017-3495-y. PMID: 28793874; PMCID: PMC5550998.
2. Waraky A, Akopyan K, Parrow V, Strömberg T, Axelson M, Abrahmsén L, Lindqvist A, Larsson O, Aleem E. Picropodophyllin causes mitotic arrest and catastrophe by depolymerizing microtubules via insulin-like growth factor-1 receptor-independent mechanism. Oncotarget. 2014 Sep 30;5(18):8379-92. doi: 10.18632/oncotarget.2292. PMID: 25268741; PMCID: PMC4226690.

In vivo study

1. Tarnowski M, Tkacz M, Zgutka K, Bujak J, Kopytko P, Pawlik A. Picropodophyllin (PPP) is a potent rhabdomyosarcoma growth inhibitor both in vitro and in vivo. BMC Cancer. 2017 Aug 9;17(1):532. doi: 10.1186/s12885-017-3495-y. PMID: 28793874; PMCID: PMC5550998.

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2. Economou MA, Andersson S, Vasilcanu D, All-Ericsson C, Menu E, Girnita A, Girnita L, Axelson M, Seregard S, Larsson O. Oral picropodophyllin (PPP) is well tolerated in vivo and inhibits IGF-1R expression and growth of uveal melanoma. Acta Ophthalmol. 2008 Nov;86 Thesis 4:35-41. doi: 10.1111/j.1755-3768.2008.01184.x. PMID: 19032680.

7. Bioactivity

Biological target:

Picropodophyllin (AXL1717) is a selective insulin-like growth factor-1 receptor (IGF-1R) inhibitor with an IC50 of 1 nM.

In vitro activity

PPP was previously reported to induce apoptosis and CDK1 is known to regulate apoptosis. In the present study PPP induced 2.5 to 3-fold increase in apoptosis compared to controls (statistically significant only in HepG2 and MCF-7 cells) (Fig. S3A, B) with reduced levels of Mcl-1 (Fig. S3C, D). In addition, PARP cleavage was observed in MCF-7 cells after 48 h of PPP treatment (Fig. S3D). To investigate whether these alterations were due to CDK1 activity, CDK1 was depleted using specific siRNA in MCF-7 cells. Depletion of CDK1 (by 80-90 %) resulted in reduced Mcl-1 levels and PARP and Caspase3 cleavage, regardless of PPP treatment (Fig. S3D). n PPP-treated HepG2 cells the percentage of pH3-positive cells increased after PPP addition to 4- and 3-fold at 8 and 24h, respectively. Similar effects were observed in Hep3B and A549 cells (Fig.4A).. The potential effect of IGF-1R on the mitotic arrest was assessed in a knock-down experiment in Hep3B cells using siRNA, showing that IGF-1R depletion did not affect the PPP-induced accumulation of cells in mitosis (Fig 4B). In conclusion, the results demonstrate a novel mechanism of action of the anticancer agent PPP, interfering with microtubule dynamics and leading to mitotic arrest

Reference: Oncotarget. 2014 Sep; 5(18): 8379–8392. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4226690/

In vivo activity

Finally, a mouse xenotransplantation model was employed. In the experiment intramuscular injections of RH30 (ARMS) cells to SCID-beige mice were performed and further divided them into two groups (control and PPP treated). A total of 10 SCID/beige mice were injected with RH30 cells (intramuscular, 6 × 106 cells per leg). After two weeks from inoculation intraperitoneal injection of PPP (40 mg/kg/24 h) and vehicle alone (50 µl DMSO) was started. It was noted, that PPP-injected mice grew significantly smaller tumours as compared to controls (Fig.7a). What is more is that bone marrow, lungs and liver were collected in order to estimate RMS cells seeding efficiency to these organs. DNA was isolated and using real-time RT-PCR, human α-satellite sequences and murine β-actin were isolated. It was found that mouse bearing RMS tumours that were treated with PPP exhibited 4 times lower amount of human cancer cells infiltrating bone marrow controls (Fig.7b). Seeding efficiency to lungs and liver was not affected by PPP treatment. What is also very important, there was no notice of significant side effects of PPP treatment, however mice injected with PPP had lower body mass (Additional file 1).

Reference: BMC Cancer. 2017; 17: 532. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5550998/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.