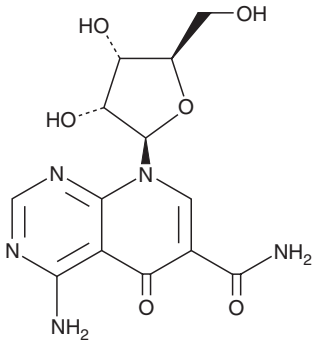
PRODUCT INFORMATION

API-1

Item No. 22081

CAS Registry No.:	36707-00-3
Formal Name:	4-amino-5,8-dihydro-5-oxo-8-β-D-ribofuranosyl-pyrido[2,3-d] pyrimidine-6-carboxamide
Synonym:	NSC 177223
MF:	$C_{13}H_{15}N_5O_6$
FW:	337.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 275, 302 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

API-1 is supplied as a crystalline solid. A stock solution may be made by dissolving the API-1 in the solvent of choice. API-1 is soluble in DMSO, which should be purged with an inert gas. The solubility of API-1 in DMSO is approximately 2 mg/ml. API-1 is also slightly soluble in dimethyl formamide.

Description

API-1 is an inhibitor of Akt that reduces the level of phosphorylated Akt (IC_{50} = ~0.8 µM in OVCAR3 cells) by binding to Akt and blocking its translocation to the cell membrane.[1] It reduces cell proliferation in various cancer cell lines, induces apoptosis, and, at a dose of 10 mg/kg per day, decreases tumor growth in a mouse xenograft model. API-1 inhibition of Akt leads to proteasomal degradation of the downstream mediator Mcl-1.[2] Likely independent of Akt binding, API-1 inhibits cell growth (IC_{50}s = 2-5 µM) and induces apoptosis in non-small cell lung and head and neck squamous cancer (NSCLC and HNSCC) cell lines with concomitant increases in caspase-3, -8, and -9 cleavage.[3] It reduces the levels of cellular FLICE-inhibitory protein (c-FLIP), an important regulator of apoptosis, through ubiquitin- and proteasome-mediated degradation. It also has a synergistic effect on apoptosis in combination with TRAIL/APO-2L.

The information regarding the reduction in phosphorylated Akt levels, IC_{50} value, translocation, cell proliferation, and xenograft tumor growth was drawn from a paper that has been retracted; however, the information specified in the retraction statement has not been included.[1]

References

1. Kim, D., Sun, M., He, L., *et al.* A small molecule inhibits Akt through direct binding to Akt and preventing Akt membrane translocation. *J. Biol. Chem.* **285(11)**, 8383-8394 (2010).
2. Ren, H., Koo, J., Guan, B., *et al.* The E3 ubiquitin ligases β-TrCP and FBXW7 cooperatively mediates GSK3-dependent Mcl-1 degradation induced by the Akt inhibitor API-1, resulting in apoptosis. *Mol. Cancer* **12(1)**, 146 (2013).
3. Li, B., Ren, H., Yue, P., *et al.* The novel Akt inhibitor API-1 induces c-FLIP degradation and synergizes with TRAIL to augment apoptosis independent of Akt inhibition. *Cancer Prev. Res. (Phila).* **5(4)**, 612-620 (2012).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM