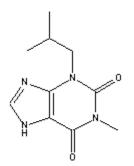
Catalog Number: 195262 3-Isobuty1-1-methylxanthine

Structure:



Molecular Formula: C₁₀H₁₄N₄O₂

Formula Weight: 222.24 (as anhydrous)

CAS #: 28822-58-4

Synonym: IBMX; MIX; MeiBu-Xan; IBX

Solubility: Soluble in Krebs-Henseleit bicarbonate buffer, ethanol (10 mg/ml or 25 mg/ml with sonication¹⁷), DMSO (1 M with warming), or aqueous NaOH (pH 9.5); slightly soluble in water (0.3 mg/ml hot water). Solubility in 45% (w/v) aqueous 2-hydroxy-propyl- β -cyclodextrin is 3.2 mg/ml. Ethanol solutions can be stored at 2-8° C for approximately three (3) months.¹⁷ DMSO solutions should be aliquoted and stored at -20° C for 3 to 4 months. Aqueous solutions can be aliquoted and stored at -20° C for approximately 3 months.²² The aqueous solutions should be thawed for use by heating in a boiling water bath.

Description: IBMX has been shown to be a potent, non-specific inhibitor of adenosine 3', 5'-cyclic monophosphate phosphodiesterase (cAMP PDE)⁴, significantly more effective than theophylline. ^{1,2,14,15,21} Also inhibits cGMP phosphodiesterases. IBMX inhibits cyclic nucleotide PDE with subsequent inhibition of cyclic nucleotide hydrolysis, resulting in accumulation of cyclic AMP and guanosine 3', 5'-cyclic monophosphate. ^{11,20} In a study of cyclic AMP and insulin release by islets of Langerhans, IBMX at 1 mM caused a marked increase in the intracellular concentration of cyclic AMP in the presence of glucose. ¹⁴

IBMX, when used at 0.05 mM, was 20-fold more effective than theophylline at stimulating lipolysis in fat cells.² It has been shown to promote the conversion of fibroblast cells into adipose cells, apparently without altering the amount of bromodeoxyuridine (BrdU) present in the DNA of the cells.¹⁶

The increase in cAMP level as a result of phosphodiesterase inhibition by IBMX activates PKA leading to decreased proliferation, increased differentiation, and induction of apoptosis. 5,7,18

Other actions of IBMX:

- Inhibition of phenylephrine-induced release of 5-hydroxytryptamine from neuroendocrine epithelial cells of the airway mucosa (IC₅₀ = 1.3 uM).⁹
- An adenosine receptor antagonist.^{7,12}
- Inhibits ion channels in the neuromuscular junction, GH3 cells, and vascular smooth muscle cells.⁸
- Inhibits the growth of carcinoma cells both in vivo and in vitro in mice.¹⁰

Pharmacology: K_i (nM): $A_1 = 2460$; $A_2 = 13800$ (ref. 6).

References:

- 1. Ashcroft, S.J.H., et al., FEBS Lett., v. 20, 263 (1973).
- 2. Beavo, J.A., et. al., Mol. Pharmacol., v. 6, 597 (1970).
- Bruns, R.F., Lu, G.H., Pugsley, T.A., "Characterization of the A₂ adenosine receptor labeled by [³H]-NECA in rat striatal membranes." *Mol. Pharmacol.*, v. 29, 331-346 (1986).
- 4. Chasin, M. and Harris, D.N., Advances in Cyclic Nucleotide Research,
 v. 7, 225-228 (1976).
- Chen, T.C., et al., "Up-regulation of the cAMP/PKA pathway inhibits proliferation, induces differentiation, and leads to apoptosis in malignant gliomas." *Lab. Invest.*, v. 78, 165-174 (1998).
- Coffin, V.L., Spealman, R.D., "Psychomotor-stimulant effects of 3-isobutyl-1-methylxanthine: comparison with caffeine and 7-(2-chloroethyl) theophylline." *Eur. J. Pharmacol.*, v. 170, 35 (1989).
- Elks, M.L. and Manganiello, V.C., "A role for soluble cAMP phosphodiesterases in differentiation of 3T3-L1 adipocytes." J. *Cell Physiol.*, v. 124, 191-198 (1985).
- 8. Fearon, I.M., et al., "Inhibition of recombinant human cardiac L-type $\rm Ca^{^{2+}}$ channel alphalC subunits by

3-isobutyl-1-methylxanthine." *Eur. J. Pharmacol.*, v. 342, 353-358 (1998).

- Freitag, A., et al., "Phosphodiesterase inhibitors suppress alpha2-adrenoceptor- mediated 5-hydroxytryptamine release from tracheae of newborn rabbits." *Eur. J. Pharmacol.*, v. 354, 67-71 (1998).
- 10. Janik, P., et al., Cancer Research, v. 40, 1950-1954 (1980).
- 11. Klotz, U., et al., Naunyn-Schmiedeberg's Archives Pharmacol., v. 296, 187 (1977).
- 12. McKinley, J.B., et al., "The interaction of adenosine analogues with cAMP-generating and cAMP-independent positive inotropic agents in rabbit left atrium." Naunyn. Schmiedebergs Arch. Pharmacol., v. 342, 605-612 (1990).
- 13. Montague, W., et. al., Biochem. J., v. 120, 9p (1970).
- 14. Montague, W., et. al., *Biochem. J.*, v. 122, 115 (1971).
- 15. Peytreman, W.E., et al., *Endocrinology*, v. 92, 525 (1973).
- 16. Russell, T. R., Proc. Natl. Acad. Sci. USA, v. 76, 4451-4454 (1979).
- 17. Schwertner, H. A., *Anal. Chem.*, v. 48, 1875 (1976).
- 18. Shafer, S.H., et al., "Reduced DNA synthesis and cell viability in small cell lung carcinoma by treatment with cyclic AMP phosphodiesterase inhibitors." *Biochem. Pharmacol.*, v. 56, 1229-1236 (1998).
- 19. Snyder, S., et. al., Proc. Natl. Acad. Sci. USA., v. 78, 3260 (1981).
- 20. Spaulding, S. W. and Burrow, G. N., *Biochem. Biophys. Res. Commun.*,
 v. 59, 386 (1974).
- 21. Data for Biochemical Research, 3rd Ed., Dawson, et al. (eds), Oxford Press, pp. 326-327 (1989).
- 22. Methods in Enzymology, v. 195, 23 (1991).