## **Product** Data Sheet

#### **IBMX**

Cat. No.: HY-12318 CAS No.: 28822-58-4 Molecular Formula:  $C_{10}H_{14}N_4O_2$  Molecular Weight: 222.24

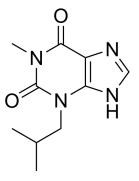
Target: Phosphodiesterase (PDE)

Pathway: Metabolic Enzyme/Protease

Storage: Powder -20°C 3 year

Powder  $-20^{\circ}$ C 3 years  $4^{\circ}$ C 2 years In solvent  $-80^{\circ}$ C 2 years

-20°C 1 year



#### **SOLVENT & SOLUBILITY**

In Vitro

DMSO: 50 mg/mL (224.98 mM; Need ultrasonic)

Ethanol : ≥ 7.14 mg/mL (32.13 mM)

\* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
	1 mM	4.4996 mL	22.4982 mL	44.9964 mL
	5 mM	0.8999 mL	4.4996 mL	8.9993 mL
	10 mM	0.4500 mL	2.2498 mL	4.4996 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- 1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility:  $\geq$  1.67 mg/mL (7.51 mM); Clear solution
- 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 1.67 mg/mL (7.51 mM); Suspended solution; Need ultrasonic
- 3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 1.67 mg/mL (7.51 mM); Clear solution
- 4. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 0.71 mg/mL (3.19 mM); Clear solution
- 5. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 0.71 mg/mL (3.19 mM); Clear solution
- 6. Add each solvent one by one: 10% EtOH >> 90% corn oil Solubility: ≥ 0.71 mg/mL (3.19 mM); Clear solution

### **BIOLOGICAL ACTIVITY**

Description	IBMX is a broad-spectrum phosphodiesterase (PDE) inhibitor, with IC $_{50}$ s of 6.5, 26.3 and 31.7 $\mu$ M for PDE3, PDE4 and PDE5, respectively.		
IC <sub>50</sub> & Target	PDE3	PDE4	
In Vitro	At 100 $\mu$ M, KMUP-1 (a xanthine derivative) and IBMX are the most effective at inducing tracheal relaxation; the magnitude of the relaxation responses induced by KMUP-1 and IBMX are not significantly different <sup>[1]</sup> . IBMX (100 $\mu$ M) activates renal outer medullary K <sup>+</sup> (ROMK) channels (n=6, P<0.05) and prevents further channel activation by ANG II (n=6, P=NS) or cGMP. Of note is that pretreatment of cortical collecting duct (CCDs) isolated from high-K <sup>+</sup> (HK)-fed rats with IBMX (100 $\mu$ M) for 20 min leads to a significant increase in tubular cAMP content to 1.43±0.35 pg/mm tubule length (n=14) compare with that measured in vehicle-treated controls (0.61±0.13 pg/mm tubule length, n=12, P<0.05) <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	IBMX, a non-selective PDE inhibitor significantly decreases the liver glycogen storage (mg/g, IBMX 22±1.5 P<0.001). In comparison with the control group, IBMX and mc5 significantly increase plasma glucose (blood glucose, mg/dl, control=141±3, IBMX=210±17 P<0.001 and mc5=191±13 P<0.01) while other test compounds (mc1, mc6, MCPIP and Win 47203) do not produce significant effect (control=141±3, mc1 160±7, mc6 175±9, MCPIP 179±8 and Win 47203 116±2 P>0.05) also mc2 does not change plasma glucose (control=141±3 and mc2=145±5). IBMX has the highest efficacy on increasing plasma glucose (3]. Treatments with IBMX and Apocynin significantly decrease cold-induced elevation of right ventricular (RV) systolic pressure (23.5±1.8 and 24.2±0.6 mmHg, respectively) although they do not decrease RV pressure to the warm control levels. IBMX or Apocynin significantly reduces medial layer thickness (19.0±0.9, and 16.9±0.8 μm, respectively) and increases lumen diameter (62.7±4.2, and 59.5±4.3 μm, respectively) of small PAs in cold-exposed rats [4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

#### **PROTOCOL**

#### Cell Assay [2]

Cells are grown in 24-well plates  $10^5$  cells per well. At confluence, monolayer cells are washed with phosphate buffer solution (PBS) and then incubated with KMUP-1 (0.1-100  $\mu$ M) in the presence of  $100~\mu$ M IBMX for 20 min. Incubation is terminated by the addition of 10% trichloroacetic acid (TCA). Cell suspensions are sonicated and then centrifuged at  $2500\times g$  for 15 min at  $4^\circ$ C. To remove TCA, the supernatants are extracted three times with 5 volumes of water-saturated diethyl ether. Then, the supernatants are lyophilized and the cyclic GMP or AMP of each sample is determined by using commercially available radioimmunoassay kits<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

# Animal Administration [3][4]

Mico[3

Male mice (25-35 g) are used. For the experiment, the test compound (IBMX, MCPIP, mc1, mc2, mc5 or mc6) or solvent (control) is injected subcutaneously to mice at 1 mg/kg dosage twice a day (8:00 a.m. and 8:00 p.m.) for 7 days.

Rats<sup>[4]</sup>

Six groups of male Sprague-Dawley rats are used (150-180g, 6 rats/group). Three groups of rats are exposed to a climate-controlled walk-in chamber maintained at moderate cold (5.0±1°C). The remaining groups are kept in an identical chamber maintained at room temperature (23.5±1°C, warm) and served as controls. After eight weeks of exposure to cold, 3 groups in each temperature condition received continuous IV infusion of IBMX (PDE-1 inhibitor, 8.5 mg/kg/day), Apocynin (NADPH oxidase inhibitor, 25 mg/kg/day) and vehicle (DMSO, 50%), respectively. The doses of drugs have been validated for effective inhibition of PDE-1 and NADPH oxidase activity, respectively. Body weight is measured weekly. After one week of drug infusion, the animals' right ventricular systolic blood pressure (RVBP) is measured under anesthesia. The RVP is a reliable indicator of pulmonary arterial blood pressure (PAP) and has been used by numerous investigators for evaluating PH.

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#### **CUSTOMER VALIDATION**

- Mol Cell. 2022 Dec 3;S1097-2765(22)01100-5.
- Clin Transl Med. 2023 Jul;13(7):e1326.
- Cancer Lett. 2022 Sep 20;215918.
- Int J Biol Sci. 2022 Apr 24;18(7):3082-3101.
- Cell Rep. 2021 Sep 21;36(12):109726.

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#### **REFERENCES**

[1]. Wu BN, et al. KMUP-1, a xanthine derivative, induces relaxation of guinea-pig isolated trachea: the role of the epithelium, cyclic nucleotides and K+ channels. Br J Pharmacol. 2004 Aug;142(7):1105-14

[2]. Wei Y, et al. Angiotensin II type 2 receptor regulates ROMK-like K+ channel activity in the renal cortical collecting duct during high dietary K+ adaptation. Am J Physiol Renal Physiol. 2014 Oct 1;307(7):F833-43

[3]. Hosseini A, et al. Differential metabolic effects of novel cilostamide analogs, methyl carbostiryl derivatives, on mouse and hyperglycemic rat. Iran J Basic Med Sci. 2012 Jul;15(4):916-25.

[4]. Crosswhite P, et al. Inhibition of phosphodiesterase-1 attenuates cold-induced pulmonary hypertension. Hypertension. 2013 Mar;61(3):585-92.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA