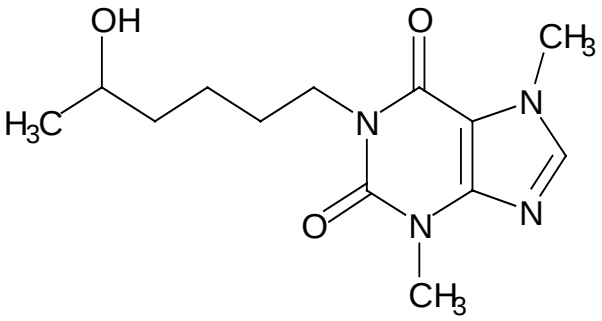
ProductInformation

LISOFYLLINE
Product Number **L 5902**
Storage Temperature RT

Cas #: 6493-06-7
Synonyms: (+/-)-1-(5-Hydroxyhexyl)-3,7-dimethyl xanthine



Product Description
Molecular Formula: $C_{13}H_{20}N_4O_3$
Molecular Weight: 280.3 (anhydrous)
Supplied as white solid
Purity: Approximately 98% by TLC

Phosphatidic acid (PA; 1,2-diacyl-sn-glycerol-3-phosphate) is the product of the degradation of membrane phosphatidylcholine by phospholipase D (PLD). PA can be further dephosphorylated to 1,2-diacyl-sn-glycerol by phosphatidate phosphohydrolase. Increases in intracellular PA and PA-derived diacylglycerol are induced by many agents including: lipopolysaccharide (endotoxin, LPS), and inflammatory cytokines (TNF-α, IL-1β).[1-3]

PA is generated by cell signaling mechanisms that activate PLD and functions as a second messenger in signal transduction pathways. It activates a family of intracellular protein kinases[4,5] and facilitates the interaction of cytoplasmic G proteins with nicotinamide adenine dinucleotide phosphate (NADPH) oxidase[6] and phospholipase Cβ1.[7] In neutrophils, the stimulation of NADPH oxidase is associated with respiratory burst activity and the generation of reactive oxygen radicals.[4,5] Phosphatidic acid is proinflammatory.

Lisofylline (LSF) is an antiinflammatory compound that selectively inhibits the formation of oleate- and linoleate-containing phosphatidic acid. LSF is a metabolite of pentoxifylline and is approximately 800-times more active than pentoxifylline as an inhibitor of PA formation in LPS-stimulated P388 monocytic leukemia cells.[1] LSF does not inhibit the activation of phosphatidylinositol-specific phospholipase C.[8] LSF protected BALB/c mice from LPS-induced lethality.[1] In rats, LSF prevented oxidant-mediated capillary leak in isolated rat lungs previously treated with IL-8. This was not due to either its anti-inflammatory activity or to the scavenging of reactive oxygen radicals. Instead, LSF appeared to alter the phospholipid composition of pulmonary capillary membranes and render this barrier less vulnerable to oxidative damage.[8] Lisofylline also protects intestinal barrier function after ischemic or hemorrhagic shock, perhaps by preserving microvascular structure and perfusion.[9,10]

Preparation Instructions
Lisofylline is soluble in DMSO.

Storage/Stability
Store at room temperature.

References

1. Rice, G.C., et al., Protection from endotoxic shock in mice by pharmacologic inhibition of phosphatidic acid., Proc. Natl. Acad. Sci. USA **91**, 3857-3861 (1994).
2. Bursten, S., et al., Potential role for phosphatidic acid in mediating the inflammatory responses to TNF-α and IL-1β. Circ. Shock **44**, 14-29 (1994).
3. Bleich, D., Lisofylline, an inhibitor of unsaturated phosphatidic acid generation, ameliorates interleukin-1 beta-induced dysfunction in cultured rat islets. Endocrinology, **11**, 4871-4877(1996).
4. English. C., et al., Messenger functions of phosphatidic acid. Chem. Phys. Lipids **80**, 117-132 (1996).
5. McPhail, L.C., et al., A novel protein kinase target for the lipid second messenger phosphatidic acid. Biochim. Biophys. Acta 1439, 277-290 (1999).
6. English, D., Phosphatidic acid: a lipid messenger involved in intracellular and extracellular signalling. Cell Signal. 8, 341-347 (1996).
7. Litosch, I., Phosphatidic acid modulates G protein regulation of phospholipase $C_{\beta 1}$ activity in membranes. Cell Signal. **14**, 259-263 (2002).
8. Guidot, D.M., et al., Modulating phosphatidic acid metabolism decreases oxidative injury in rat lungs. Am. J. Physiol. **273**, L957-L966 (1997).

9. Wattanasirichaigoon, S., et al., Lisofylline ameliorates intestinal mucosal barrier dysfunction caused by ischemia and ischemia/reperfusion., Shock, **11,** 269-275 (1999).

10. Wattanasirichaigoon, S., et al., Lisofylline ameliorates intestinal and hepatic injury induced by hemorrhage and resuscitation in rats. Crit. Care Med. **28**, 1540-1549 (2000).

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