

PRODUCT INFORMATION



KMN-80

Item No. 15435

Issued United States Patent US 9,688,627 and all US and foreign patents pending related to PCT Publ. No. WO 2014/144584.

CAS Registry No.: 1628759-75-0

Formal Name: 7-((R)-2-((3S,4S,E)-3-hydroxy-4-methylnon-1-en-6-yn-1-yl)-5-oxopyrrolidin-1-yl)heptanoic acid

MF: $C_{21}H_{33}NO_4$

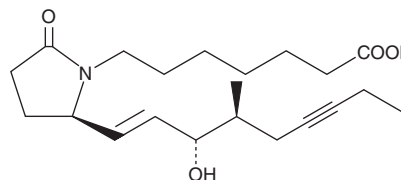
FW: 363.5

Purity: $\geq 98\%$

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

KMN-80 is supplied as a crystalline solid. A stock solution may be made by dissolving the KMN-80 in the solvent of choice, which should be purged with an inert gas. KMN-80 is soluble in the organic solvent DMSO at a concentration of approximately 10 mg/ml.

Description

The prostaglandin E receptor 4 (EP_4) is one of four G protein-coupled receptors that mediate the actions of prostaglandin E_2 (PGE_2 ; Item No. 14010). Binding of PGE_2 to the EP_4 receptor causes an increase in intracellular cyclic AMP, which plays important roles in bone formation and resorption, cancer, and atherosclerosis.¹⁻⁴ KMN-80 is a substituted γ -lactam (pyrrolidinone) derivative of PGE_1 (Item No. 13010) that acts as a selective and potent agonist of EP_4 with an IC_{50} value of 3 nM ($IC_{50} = 1.4 \mu\text{M}$ for EP_3 and $> 10 \mu\text{M}$ for all other prostanoid receptors).⁵ In functional assays it has been shown to stimulate secreted alkaline phosphatase gene reporter activity in EP_4 -transfected HEK293 cells with an EC_{50} value of 0.19 nM, demonstrating $>5,000$ and $50,000$ -fold selectivity against EP_2 and TP, respectively.⁵ KMN-80 can induce the differentiation of bone marrow stem cells from both young and aged rats into osteoblasts *in vitro* (EC_{50} s = 20 and 153 nM, respectively) and exhibits favorable tolerability up to at least $10 \mu\text{M}$, whereas the EP_4 agonist L-902,688 (Item No. 10007712) is highly cytotoxic at similar concentrations in these cells.⁶ KMN-80 has been used to repair calvarial defect in an *in vivo* rat craniomaxillofacial reconstruction model (rate of reduction in defects size equivalent to BMP-2 treated rats) and to promote bone formation in a rat incisor tooth socket model.⁶

References

1. Li, M., Thompson, D.D., and Paralkar, V.M. *Int. Orthop.* **31**, 767-772 (2007).
2. Hawcroft, G., Ko, C.W.S., and Hull, M.A. *Oncogene* **26**, 3006-3019 (2007).
3. Babaev, V.R., Chew, J.D., Ding, L., et al. *Cell Metab.* **8**, 492-501 (2008).
4. Konya, V., Marsche, G., Schuligoi, R., et al. *Pharmacol. Ther.* **138**(3), 485-502 (2013).
5. Barrett, S.D., Ciske, F.L., Endres, G.W., et al. Novel Potent Lactam Acetylene EP_4 Agonists Stimulate Alkaline Phosphatase Production and Differentiation in Bone Marrow Cells, (2014).
6. O'Malley, J., Uzieblo, A., Germain, B.D., et al. Development of a Novel Prostaglandin EP_4 Agonist Which Stimulates Local Bone Formation *in vivo*, (2014).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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