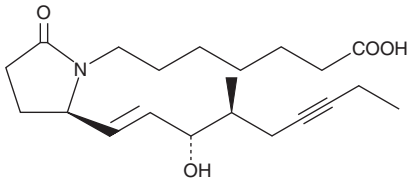
PRODUCT INFORMATION

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: ≥98%
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥1 year



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 µM for EP_3 and > 10 µM 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 µM, 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

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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).

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