

Madindoline A

A Potent Inhibitor of Interleukin-6 [IL-6]

highlight

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International Version

NEW

(+)-Madindoline A

[[[(2R, 3aR, 8aS)-8-[4-(n-Butyl)-2,5-dimethyl-1,3-dioxo-2-(4-cyclopentyl)methyl]-3,3a,8,8a-tetrahydro-3a-hydroxy-2H-furo[2,3-b]indole]

ALX-350-328-MC05 0.5 mg

ALX-350-328-M001 1 mg

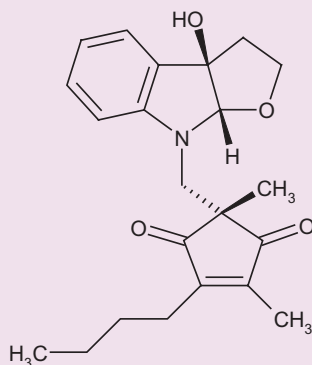
FORMULA: C₂₂H₂₇NO₄

MW: 370.2 T

PURITY: ≥97%

SOLUBILITY: Soluble in methanol or 100% ethanol; insoluble in hexane.

LONG TERM STORAGE: -20°C



Manufactured by the
Kitasato Institute, Tokyo.

Introduction

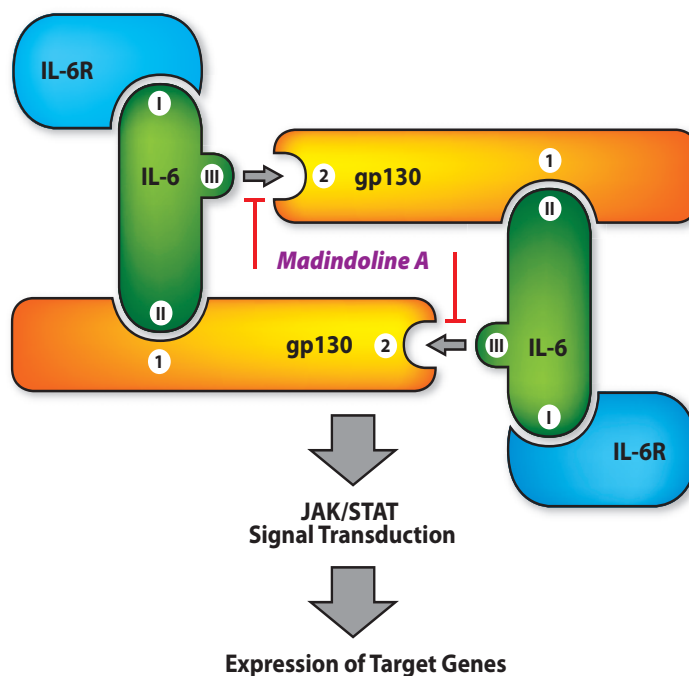


FIGURE 1: Madindoline A inhibits homodimerization of the two trimeric IL-6 / IL-6R / gp130 complexes by binding to site 2 of gp130.

Madindolines are noncytotoxic indole alkaloids originally isolated from a fermentation broth of *Streptomyces nitrosporeus* K93-0711 [1, 2]. (+)-Madindoline A (MadA; MDL-A) and (+)-Madindoline B (MadB; MDL-B) are diastereomers with MadA being the more potent compound. MadA binds competitively but noncovalently to the extracellular domain of the membrane glycoprotein gp130 and inhibits the homodimerization of the trimeric IL-6/IL-6R/gp130 or the IL-11/gp130 complex [1-3], thus inhibiting activation of the JAK/STAT signal transduction pathway [4]. MadA inhibits IL-6 and IL-11-induced osteoclastogenesis *in vitro* in a dose dependent manner and postmenopausal

osteoporosis *in vivo*, by a mechanism different from that of 17β-estradiol [5]. IL-6 activity is known to cause various diseases such as cancer cachexia [6], Castleman's disease [7], Crohn's disease [8], rheumatoid arthritis [9], hypercalcemia [10], and multiple myeloma [11]. Madindolines are no longer available from natural sources due to mutation of the originating bacterial strain. Thus, synthetic routes have been developed to produce madindolines [12]. Recently analogs of madindolines have been synthesized as potent IL-6 inhibitors [13].

FOR LITERATURE REFERENCES SEE BACKCOVER

Literature References

[1] Madindoline, a novel inhibitor of IL-6 activity from Streptomyces sp. K93-0711. I. Taxonomy, fermentation, isolation and biological activities: M. Hayashi, et al.; J. Antibiot. **49**, 1091 (1996) • [2] Madindolines, novel inhibitors of IL-6 activity from streptomyces sp. K93-0711. II. Physico-chemical properties and structural elucidation: S. Takamatsu, et al.; J. Antibiot. **50**, 1069 (1997) • [3] Binding of madindoline A to the extracellular domain of gp130: A.Z. Saleh, et al.; Biochemistry **44**, 10822 (2005) [4] Association of transcription factor APRF and protein kinase Jak1 with the interleukin-6 signal transducer gp130: C. Lutticken, et al.; Science **263**, 89 (1994) • [5] Suppression of bone resorption by madindoline A, a novel non-peptide antagonist to gp130: M. Hayashi, et al.; PNAS **99**, 14728 (2002) • [6] Mechanisms of experimental cancer cachexia. Local involvement of IL-1 in colon-26 tumor: G. Strassmann, et al.; J. Immunol. **150**, 2341 (1993) [7] Pathogenic significance of interleukin-6 (IL-6/BSF-2) in Castleman's disease: K. Yoshizaki, et al.; Blood **74**, 1360 (1989) • [8] Inhibition of IL-6 for the treatment of inflammatory diseases: N. Nishimoto & T. Kishimoto; Curr. Opin. Pharmacol. **4**, 386 (2004) • [9] Blockage of interleukin-6 receptor ameliorates joint disease in murine collagen-induced arthritis: N. Takagi, et al.; Arthritis Rheum. **41**, 2117 (1998) • [10] Interleukin-6 enhances hypercalcemia and bone resorption mediated by parathyroid hormone-related protein in vivo: J. de la Mata, et al.; J. Clin. Invest. **95**, 2846 (1995) • [11] Granulocyte-macrophage colony-stimulating factor synergizes with interleukin-6 in supporting the proliferation of human myeloma cells: X.G. Zhang, et al.; Blood **76**, 2599 (1990) • [12] Synthesis of (+)-madindoline A and (+)-madindoline B: L. Wan & M.A. Tius; Org. Lett. **9**, 647 (2007) • [13] Design, synthesis, and biological activities of madindoline analogues: D. Yamamoto, et al.; Bioorg. Med. Chem. Lett. **16**, 2807 (2006)

Monoclonal Antibodies to Phosphorylated STAT1 & STAT3

MAb to STAT1 (human) (phosphorylated) (pSer⁷²⁷) (PSM1)

ALX-804-577-C100 **100 µg**
CLONE: PSM1. ISOTYPE: Mouse IgG1. IMMUNOGEN: Synthetic peptide corresponding to aa 721-733 (D⁷²¹NLLPMPSPPEFDE⁷³³) of human STAT1 phosphorylated at Ser⁷²⁷. SPECIFICITY: Recognizes human STAT1. APPLICATION: IP, WB.

LIT: Malignant melanoma associates with deficient IFN-induced STAT1 phosphorylation: J. Kovarik, et al.; Int. J. Mol. Med. **12**, 335 (2003)

MAb to STAT1 (human) (phosphorylated) (pSer⁷²⁷) (12C5)

NT-0176-100 **100 µg**
CLONE: 12C5. ISOTYPE: Mouse IgG1. IMMUNOGEN: Synthetic peptide corresponding to a portion of STAT1 phosphorylated at Ser⁷²⁷. SPECIFICITY: Recognizes human STAT1 phosphorylated at Ser⁷²⁷. Does not cross-react with non-phosphorylated STAT1. APPLICATION: WB.

MAb to STAT3 (phosphorylated) (pTyr⁷⁰⁵) (9E12)

ALX-804-180-C100 **100 µg**
CLONE: 9E12. ISOTYPE: Mouse IgG1. IMMUNOGEN: Synthetic peptide corresponding to a portion of STAT3 phosphorylated at Tyr⁷⁰⁵. SPECIFICITY: Recognizes the -AAPpYLKT-motif of activated human, mouse and dog STAT3 phosphorylated at Tyr⁷⁰⁵. Does not cross-react with the non-phosphorylated form of STAT3 nor with unrelated tyrosine-phosphorylated proteins. APPLICATION: IHC, ICC, IP, WB.

Related Products

STATs

STAT1 (human) (rec.)

JBS-PR-862 **10 µg**
Produced in insect cells.

MAb to STAT1 (human) (SM2)

ALX-804-576-C100 **100 µg**
CLONE: SM2. ISOTYPE: Mouse IgG1. IMMUNOGEN: Synthetic peptide corresponding to aa 9-23 (Q⁹LD-SKFLEQVHQLYD²³) of human STAT1. SPECIFICITY: Recognizes human STAT1. APPLICATION: IP, WB.

PAb to STAT1α

PSC-1021-C100 **100 µg**
From rabbit. IMMUNOGEN: Synthetic peptide corresponding to aa 712-750 of human STAT1α. SPECIFICITY: Recognizes human, mouse and rat STAT1α. Detects a band of ~91kDa by Western blot. Does not cross-react with STAT1β. APPLICATION: IP, WB. BP: PSC-1021P.

Interleukin-6 [IL-6] & Antibodies

IL-6 (human) (rec.)

BMS341 **20 µg**
Produced in *E. coli*.

MAb to IL-6 (human) (B-E8)

BMS130 **100 µg**
BMS130FI **FITC** **100 tests**
CLONE: B-E8. ISOTYPE: Mouse IgG1. SPECIFICITY: Recognizes human IL-6 (interleukin-6). APPLICATION: FC, ICC. FUNC: Neutralizing.

MAb to IL-6 (mouse) (6B4 IGH 54)

ALX-804-335-C100 **100 µg**
CLONE: 6B4 IGH 54. ISOTYPE: Rat IgG1. IMMUNOGEN: Recombinant mouse IL-6 (interleukin-6). SPECIFICITY: Recognizes mouse IL-6. APPLICATION: ELISA. FUNC: Neutralizing.

MAb to IL-6 Receptor (human) (B-R6)

BMS135 **100 µg**
BMS135BT **Biotin** **100 tests**
CLONE: B-R6. ISOTYPE: Mouse IgG1. SPECIFICITY: Recognizes the gp80 chain of human IL-6 receptor (IL-6R). APPLICATION: FC. FUNC: Neutralizing.

Interleukin-6 [IL-6] ELISA Kits

IL-6 (human) ELISA Kit

BMS213/2 **1 Kit**
BMS213INST **Instant** **1 Kit**

For the quantitative detection of human IL-6 in cell culture supernatants, human serum, plasma, urine, synovial fluid, amniotic fluid or other body fluids. QUANTITY: 96 wells (~80 tests). SENSITIVITY: 0.92pg/ml.

IL-6 (human) ELISA Kit (High Sensitivity)

BMS213HS **1 Kit**

For the quantitative detection of human IL-6 in cell culture supernatants, human serum, plasma, urine, synovial fluid, amniotic fluid or other body fluids. QUANTITY: 96 wells (~80 tests). SENSITIVITY: 0.02pg/ml.

IL-6 (monkey) Instant ELISA Kit

BMS641INST **1 Kit**

For quantitative detection of monkey IL-6 in cell culture supernatants, monkey serum, plasma, urine, synovial fluid, amniotic fluid or other body fluids. QUANTITY: ~128 tests. SENSITIVITY: 1.5U/ml.

IL-6 (mouse) ELISA Kit

BMS603 **1 Kit**

For the quantitative detection of mouse IL-6 in cell culture supernatants, mouse serum, plasma or other body fluids. QUANTITY: 96 wells (~80 tests). SENSITIVITY: 7.92pg/ml.

IL-6 (rat) ELISA Kit

BMS625 **1 Kit**

For the quantitative detection of rat IL-6 in cell culture supernatants, rat serum, plasma or other body fluids. QUANTITY: 96 wells (~80 tests). SENSITIVITY: 12.0pg/ml.

IL-6 Receptor, Soluble (human) ELISA Kit

BMS214 **1 Kit**
BMS214INST **Instant** **1 Kit**

For the quantitative detection of soluble human IL-6 receptor levels in cell culture supernatants, human serum, plasma, urine, amniotic fluid or other body fluids. QUANTITY: 96 wells (~80 tests). SENSITIVITY: 0.01ng/ml.



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