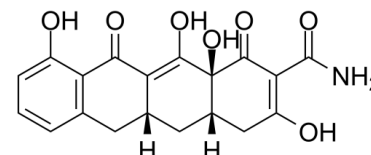


## Data Sheet

|                           |   |
|---------------------------|---|
| <b>Product Name:</b>      | Incyclinide                                     |
| <b>Cat. No.:</b>          | CS-7504   |
| <b>CAS No.:</b>           | 15866-90-7                                      |
| <b>Molecular Formula:</b> | C <sub>19</sub> H <sub>17</sub> NO <sub>7</sub> |
| <b>Molecular Weight:</b>  | 371.34  |
| <b>Target:</b>            | MMP   |
| <b>Pathway:</b>           | Metabolic Enzyme/Protease                       |
| <b>Solubility:</b>        | DMSO : ≥ 100 mg/mL (269.29 mM)                  |



### BIOLOGICAL ACTIVITY:

Incyclinide (CMT-3, COL-3) is a matrix metalloproteinase (MMP) inhibitor, thereby inducing extracellular matrix degradation, and inhibiting angiogenesis, tumor growth and invasion, and metastasis. **In Vitro:** Incyclinide has been shown to experimentally suppress prostate cancer, colon adenocarcinoma and melanoma invasiveness in cell culture. Adding incyclinide at final concentrations of 5 to 20  $\mu$ M inhibits MT1-MMP gelatinolytic and caseinolytic activity, blocks MT1-MMP activation of pro-MMP-2, and decreases invasiveness of HT-1080 fibrosarcoma cells<sup>[1]</sup>. Incyclinide is an especially effective inhibitor of the growth and viability of filamentous fungi. Most of the MICs of CMT-3 against filamentous fungi are found to be between 0.25 and 8  $\mu$ g/mL, and the inhibition of viability of these fungi by incyclinide is routinely higher than 90%<sup>[2]</sup>. **In Vivo:** Incyclinide inhibits tooth movement in the rat, probably by reducing the number of osteoclasts at the compression side. This might be due to induction of apoptosis in activated osteoclasts or reduced osteoclast migration. Reduced MMP activity by incyclinide might also directly inhibit degradation of the organic bone matrix<sup>[3]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** <sup>[2]</sup>Determination of *C. albicans* growth inhibition by CMT-3 is carried out by a modified turbidity assay. A series of tubes containing PDB (5 mL) and different concentrations of incyclinide (0, 0.125, 0.25, 0.5, 1.0, and 2.0  $\mu$ g/mL) are each inoculated with a 100  $\mu$ L suspension of *C. albicans* in late log phase to yield a final cell concentration of  $10^6$ /mL. The tubes are aerobically incubated at 35°C, and at each time point (0, 1, 2, 4, 6, 12, and 24 h), the turbidity in each tube is determined spectrophotometrically at 600 nm<sup>[2]</sup>.

**Animal Administration:** <sup>[3]</sup>Rat: Eighteen Wistar rats receive a standardized orthodontic appliance at one side of the maxilla. During 14 days, three groups of six rats receive a daily dose of 0, 6 or 30mg/kg incyclinide, and tooth displacement is measured. Thereafter, osteoclasts are counted on histological sections using an ED-1 staining. Multi- and mononuclear ED-1-positive cells in the PDL are also counted. In addition, sections are stained for MMP-9<sup>[3]</sup>.

### References:

- [1]. Lee HM, et al. CMT-3, a non-antimicrobial tetracycline (TC), inhibits MT1-MMP activity: relevance to cancer. *Curr Med Chem*. 2001 Feb;8(3):257-60.
- [2]. Liu Y, A chemically modified tetracycline (CMT-3) is a new antifungal agent. *Antimicrob Agents Chemother*. 2002 May;46(5):1447-54.
- [3]. Bildt MM, et al. CMT-3 inhibits orthodontic tooth displacement in the rat. *Arch Oral Biol*. 2007 Jun;52(6):571-8.

### CAIndexNames:

2-Naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, (4aS,5aR,12aS)-

**SMILES:**

O=C(C(C1=O)=C(O)C[C@]2([H])C[C@]3([H])CC4=C(C(C3=C(O)[C@@]21O)=O)C(O)=CC=C4)N

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

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