P08 Gelastatins, New Inhibitors of Matrix Metalloproteinases from *Westerdykella multispora* F50733

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Matrix metalloproteinases (MMPs) are a family of zinc-dependent proteases that degrade extracellular matrix and basement membrane. These enzymes are play important roles in tumor cell invasion and metastasis, as well as angiogenesis and other connective tissue diseases. In our screening program for inhibitors of MMP-2 from fungal metabolites, we have isolated novel non-peptidic inhibitors of MMPs, designated gelastatin A and B from the culture broth of *Westerdykella multispora* F50733. The structures of gelastatin A and B were determined to be 3-(5*E*-hexa-2*E*,4*E*-dienylidene-2-oxo-5,6-dihydro-2H-pyran-3yl)-propanoic acid and 3-(5*Z*-hexa-2*E*,4*E*-dienylidene-2-oxo-5,6-dihydro-2H-pyran-3yl)-propanoic acid, respectively. Gelastatin A and B exist as a mixture of two stereoisomers in a ratio of 2:1. The 2:1 mixture of gelastatin A and B inhibited activated MMP-2 and MMP-9 with an IC_{50} value of 0.63, 5.29 μM, respectively. They inhibited the invasion of B16F10 melanoma cells through basement membrane Matrigel with dose dependent.